

Attorney Docket No.: DWW-5001

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Rotin et al.

Serial No.: 09/911,826

Group Art Unit: 1636

Filed: July 20, 2001

Examiner: Q. Nguyen

For: RAS ACTIVATOR NUCLEIC ACID MOLECULES, POLYPEPTIDES AND
METHODS OF USE

Confirmation No.: 9258

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
Washington, D.C. 20231

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Sir:

In accordance with 37 C.F.R. 1.56, 1.97 and 1.98, Applicants submit herewith references which they believe may be material to the patentability of this application and with respect to which there may be a duty to disclose in accordance with 37 C.F.R. 1.56.

While the references may be "material" under 37 C.F.R. 1.56, it is not intended to constitute an admission that the references are "prior art" unless specifically designated as such.

The filing of this Information Disclosure Statement shall not be construed as a representation that no other material references than those listed exist or that a search has been conducted.

The references are listed in PTO form 1449 which is in accordance with the requirements of M.P.E.P. 609. A copy of the references is also enclosed. References cited in the PCT search report are asterisked. A copy of the PCT report is also enclosed.

The references are as follows:

1. Nagase T et al. "Prediction of the Coding Sequences of Unidentified Human Genes. VII. The Complete Sequences of 100 New cDNA Clones from Brain Which Can Code for Large Proteins *in vitro*." DNA RESEARCH, vol. 4, no.4, 1997, pgs. 141-150.*
2. Chen L et al. "A Murine CDC27/*ras*-GRF-Related Protein Implicated in Ras Regulation." Developmental Genetics, vol. 14, no. 5, 1993, pgs. 339-346.*
3. Cen H et al. "Regulated and Constitutive Activity by CDC25Mm (GRF), a Ras-Specific Exchange Factor." Molecular and Cellular Biology, vol. 13, no. 12, 1993, pgs. 7718-7724.*
4. Tung P S et al. "A 54-kDa Protein related to ras-guanine nucleotide release factor expressed in the rat exocrine pancreas." Cell and Tissue Research, vol. 289, no. 3, 1997, pgs. 505-515.*
5. Pearsall R S et al. "A Direct Repeat Sequence at the *Rasgrf1* Locus and Imprinted Expression." Genomics, vol. 55, 1999, pgs. 194-201.*
6. Brambilla R et al. "Disruption of the Ras exchange factor gene, *RasGRF/CD25*, reveals a role for Ras signaling in learning and memory." Society for Neuroscience, vol. 22, 1996, pg. 1935.*
7. Pham N et al. "The guanine nucleotide exchange factor *CNrasGEF* activates Ras in response to cAMP and cGMP." Current Biology, vol. 10, no. 9, 2000, pgs. 555-558, S1-S3.
8. Otsuka T et al. "nRap GEP: A Novel Neural GDP/GTP Exchange Protein for Rap1 Small G Protein That Interacts with Synaptic Scaffolding Molecule (S-SCAM)." Biochemical and Biophysical Research Communications, vol. 265, no. 1, 1999, pgs. 38-44.

9. de Rooij J et al. "PDZ-GEF1, a Guanine Nucleotide Exchange Factor Specific for Rap1 and Rap2." *The Journal of Biological Chemistry*, vol. 274, no. 53, 1999, pgs. 38125-38130.
10. Weisskopf M G et al. "Mediation of Hippocampal Mossy Fiber Long -Term Potentiation by Cyclic AMP." *Science*, vol. 265, 1994, pgs. 1878-1882.
11. Iyengar R. "Gating by Cyclic AMP: Expanded Role for an Old Signaling Pathway." *Science*, vol. 271, 1996, pgs. 461-463.
12. Shabb, J B et al. "Cyclic Nucleotide-binding Domains in Proteins Having Diverse Functions." *The Journal of Biological Chemistry*, vol. 267, no. 9, 1999, pgs. 5723-5726.
13. Taylor S S. "cAMP-dependent Protein Kinase." *The Journal of Biological Chemistry*, vol. 264, no. 15, 1989, pgs. 8443-8446.
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15. Weber I T et al. "Predicted Structures of cAMP Binding Domains of Type I and II Regulatory Subunits of cAMP-Dependent Protein Kinase." *Biochemistry*, vol. 26, no. 2, 1987, pgs. 343-350.
16. Dawnward J. "New exchange, new target." *Nature*, vol. 396, 1998, pgs. 416-417.
17. Kawasaki H et al. "A Family of cAMP-Binding Proteins That Directly Activate Rap1." *Science*, vol. 282, 1998, pgs. 2275-2279.
18. de Rooij J et al. "Epac is a Rap1 guanine-nucleotide-exchange factor directly activated by

cyclic AMP." Nature, vol. 396, 1998, pgs. 474-477.

19. Bailey C H et al. "Toward a molecular definition of long-term memory storage." Proc. Natl. Acad. Sci., vol. 93, 1996, pgs. 13445-13452.

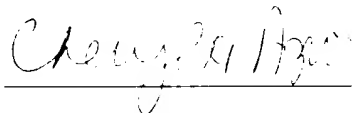
20. Hammerschmidt M et al. "Protein kinase A is a common negative regulator of Hedgehog signaling in the vertebrate embryo." Genes and Development, vol.10, 1996, pgs. 647-658.

21. Ohara O. "AB002311. Human mRNA for KIAA0313[gi:2224566]." Direct Submission, published in 1997.

It is respectfully requested that these references be considered by the Patent and Trademark Office in its examination of the above-identified application and be made of record therein. The Examiner is also invited to contact the Undersigned if there are any questions concerning this paper or the attached references.

Respectfully submitted,

Date: 1/14/03



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